DEPARTMENT OF HEALTH AND HUMAN SERVICES

5/10/00 M31490

Food and Drug Administration
Kansas City District
Southwest Region
P.O. Box 15905
Lenexa, Kansas 66285-5905

Telephone: (913) 752-2100

May 9, 2000

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER
KAN #2000-16

Mr. Marc S. Hermelin
Vice Chairman
and Chief Executive Officer
KV Pharmaceutical Company
2303 Schuetz Road
Maryland Heights, MO 63146

Dear Mr. Hermelin:

Investigators from our office found significant deviations from Current Good Manufacturing Practice (CGMP) regulations during inspection of your drug manufacturing operations on February 7, 2000 to March 3, 2000. The deviations cause drugs you manufacture to be adulterated under Section 501(a)(2)(b) of the Federal Food, Drug and Cosmetic act (the Act). CGMP regulations applicable to operations covered during the inspection are in Title 21, Code of Federal Regulations, Parts 210 and 211 (21 CFR 210 and 211).

The following drug manufacturing sites of your firm were inspected: 2302 Schuetz Road, Maryland Heights, MO; 2503 South Hanley Road, St. Louis, MO; 10858 Metro Court, Maryland Heights, MO; 10888 Metro Court, Maryland Heights, MO; 2525 Hanley Road, St. Louis, MO; 8046/8050 Litzsinger Road, St. Louis, MO; 819 Hanley Industrial Court, St. Louis MO. Some of the CGMP deviations we found include the following:

> You did not follow KV SOP 211.194.01, which unconditionally prohibits overwriting of test data entries. Your repeated failure to follow this procedure in supervisory review of raw material analytical data resulted in acceptance and use of raw materials that failed to meet specifications. [21 CFR 211.80(a)]
>
> You did not develop and use effective foreign material detection procedures in manufacturing Butoconazole Nitrate Cream. [21 CFR 211.100(a)]

You should not consider the above deficiencies as an all-inclusive list of violations that may be present in your operations. You are responsible for ensuring compliance with all requirements of the Act, and all associated regulations. If we find that violations continue, we may initiate regulatory action such as seizure and/or injunction without further notice. We advise other Federal agencies when Warning Letters about drugs and devices are issued so they may take that information into account when awarding contracts.

We have enclosed a copy of Form FDA 483, Inspectional Observations, issued to Mr. Eric Moyerman at the conclusion of our inspection. We received Ms. Janet L. Negele's letter of March 16, 2000 responding to the FDA 483. We found her commitments to corrective actions generally adequate, however we have comments on three issues.

In regard to observations concerning improper employee data reporting, we concur in your internal investigation and follow-up corrective actions. However, it is probable you would have detected the situation sooner if the SOP concerning overwriting of data had been followed, and as a result, questionable data would not have been involved in the New Drug Application submission.

We do not have objections to your validation protocol covering the visual test for foreign material detection in Butoconazole Nitrate Cream. However, before developing this procedure, you released 13 batches of this drug, 12 of which were subsequently found to contain fibers, Teflon, paint chips and other particulate matter. After you knew about this contamination, your only corrective action prior to our inspection consisted of identifying and eliminating potential sources of contamination. You should have developed an effective detection procedure as soon as the problem was known in order to verify that all sources of contamination had been found and corrected.

Ms. Negele's response to FDA 483 Observation Number 9 reports evaluation of endpoint correction evaluation for automated silver nitrate titration assay of Potassium Chloride Extended Release Capsules. KV Method 5128.10 authorizes either manual or automated titration for the assay procedure: however, Ms. Negele's response does not address endpoint evaluation of the manual method.

If, as a result of this letter, you wish to add further comments, or additional information to your response to the FDA 483, those should be directed to Noel G. Ferguson, Compliance Officer at the address shown in this letterhead.

Sincerely,

Mary Woleske

Mary Woleske
Acting District Director
Kansas City District